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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/731,657	03/12/2001	Caroline Osterhoff	35-196	1569

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EXAMINER
ULM, JOHN D

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/731,657	Osterhoff et al.
Examiner	**Art Unit**
John Ulm	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 23, 2002*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above, claim(s) *6-16, 18-20, and 23-30* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-5, 17, 21, and 22* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *13*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1) Claims 1 to 30 are pending in the instant application.

2) Claims 6 to 16, 18 to 20 and 23 to 30 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

3) Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4) The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5) Claims 1 to 5, 17, 21 and 22 stand rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed specific and substantial credible utility for those reasons of record in section 3 of Paper Number 11.

Applicant's assertion that the instant rejection is in conflict with those utility guidelines executed on 03 July of 1995 completely ignores the subsequent "REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS" (http://ptoweb.uspto.gov/patents/filecab/documents/Utility.pdf - 188.0KB, 28 Feb. 2000) upon which the instant rejection is based and which Applicant is encouraged to review. Applicant has failed to identify any inconsistency between those subsequent guidelines and the instant rejection.

Applicant urges that Applicant's own peer reviewed publication Osterhoff et al. (DNA and Cell Biol. 16(4):379-389, Apr. 1997) does not support the instant rejection because "further

work, such as a reasonable amount of experimentation, may always be required or even "essential", presumably, to establish a disclosed utility. To the contrary, it is a matter of law that an invention must have a practical utility in currently available form (at the time that an application for a patent is filed). The law does not permit further experimentation for the purpose of identifying or establishing a specific utility for the claimed invention because, if further experimentation is needed, then the invention was not useful in currently available form. The assertion that a protein of the instant invention is involved in male fertility does not constitute or support a specific and substantial utility if one must engage in further experimentation to determine **how** that protein is involved in male fertility. Because a protein of the instant invention belongs to the G protein-coupled receptor family and members of this family induce and inhibit a variety of cellular response upon activation, one would have no way of predicting what effects the activation of the claimed protein will have on epididymis. It is possible that a agonist of the claimed protein may enhance fertility, reduce fertility, or have no effect at all upon fertility. As such, the employment of a protein of the instant invention in the identification of agonists and antagonists thereto is of no practical utility until one has **completed** the experimentation necessary to determine what specific role, if any, that a protein of the instant invention plays in male fertility.

Applicant has traversed the instant rejection on the premise that the instant specification discloses a substantial utility for the claimed protein in the "diagnosis and treatment of male infertility". As stated in the original rejection "the instant specification does not provide evidence

or a credible line of reasoning which supports a conclusion that the administration of a protein of the instant invention to an individual would result in an immune response or that such an immune response would be contraceptive" and "[t]here is also a complete lack of evidence that a receptor protein of the instant invention is the target of auto-antibodies which are causative of infertility, as suggested on page 13 of the instant specification".

Applicant has further traversed the instant rejection on the premise that the employment of a protein of the instant invention as an epididymis tissue marker is a specific and substantial utility. The production of subtractive libraries to isolate cDNAs encoding proteins which are expressed in a tissue-specific or developmentally-specific manner was a practice that was old to the art of molecular biology by the time that the instant invention was made. It is now believed in the art that the human genome encodes approximately 30,000 protein, of which only about 5,000 are "housekeeping" proteins which are not expressed in a tissue-specific or developmentally-specific manner. This means that five out of six proteins in the human body are expressed in a tissue-specific or developmentally-specific manner and the isolation of a cDNA encoding a protein having a desired tissue expression pattern requires nothing more than the routine practice of the art. Therefore, the employment of a particular protein simply as a marker for the tissue in which it is expressed is no more of a specific and substantial utility than the employment of that protein as a molecular weight marker in an analytical process simply because it has a molecular weight which is different from the molecular weights of most other proteins.

The declaration by Ulrich Gotwald under 37 CFR 1.132 which was filed 18 January of 2003 is insufficient to overcome the rejection of claims 1 to 5, 17, 21 and 22 based upon a lack of specific and substantial utility as set forth in the last Office action because it fails to establish a specific and substantial utility for the claimed protein in currently available form. This declaration described the production of transgenic mice in which the murine ortholog of the claimed protein has been eliminated. This declaration shows that the complete abolition of a protein of the instant invention from a male mammal results in a reduction in the fertility of that mammal. This evidence does not appear to support a conclusion that the administration of a protein of the instant invention, or antibodies thereto, to a mammal will effect the fertility of that mammal.

The protein of the instant invention is a member of the G protein-coupled receptor family. There is not a single reference of record describing the administration of a G protein-coupled receptor or antibodies to a G protein-coupled receptor to an organism to achieve a clinical effect. At best, one of ordinary skill in the art would conclude from the Gotwald declaration that a protein of the instant invention may serve as a target for antagonists thereto, which might be expected to reduce the fertility of a male mammal to which they were administered. However, before one can identify an antagonist to the claimed protein one must know the identity of at least one agonist to that receptor protein and at least one measurable physiological parameter which is influenced by the binding of that agonist to the receptor. Unless one can measure the activity of the claimed protein one can not identify compounds which inhibit that activity (antagonists). Therefore, one would conclude that a protein of the instant invention will ultimately have the

practical utility of being employed to identify compounds which reduce male fertility. However, a claimed invention must have a practical utility in currently available form and a protein of the instant invention can not be employed to identify antagonists thereto until one has made the substantial inventive contribution of discovering the identity of at least one agonist to that receptor protein and at least one measurable physiological parameter which is influenced by the binding of that agonist to the receptor.

Further, one would not reasonably expect that the administration of an antibody to a protein of the instant invention to an individual would result in a reduction of that individual's fertility. The Chuntharapai et al. publication (Methods in Enzymology 288:15-27, 1997, cited by Applicant) describes the production of antibodies to that class of G protein-coupled receptors known as the chemokine receptors. This reference discloses that the production of "blocking" antibodies, which prevent the activation of a selected receptor by its respective ligand, was only accomplished by immunizing a mouse with a cell expressing the selected receptor and then screening the subsequently produced monoclonal antibodies for those which could actually antagonize that receptor. This reference shows that most of the antibodies produced against a particular G protein-coupled receptor will not antagonize that receptor. It supports the conclusion that an artisan must know the identity of at least one agonist to a receptor protein and at least one measurable physiological parameter which is influenced by the binding of that agonist to the receptor before that artisan can identify those antibodies in a hybridoma library which are antagonistic for a given receptor.

Any assertion that the knock-out mice described in the Gotwald declaration are representative of a naturally occurring disease or disorder would not be supported by the evidence of record. The fact that one can create a tissue-specific disorder by eliminating a tissue-specific gene product does not support a conclusion that a naturally occurring disorder reflecting a similar disfunction is the consequence of a similar genetic defect. It is well known in the art that different forms of diseases such as hepatitis and meningitis have common symptoms resulting from diverse causes. There is no evidence currently of record that a reduced fertility in certain human males results from an altered structure or pattern of expression of a protein of the instant invention. Further, Applicant's argument that the detection of a protein of the instant invention in a sample can be employed to quantitate e epididymis and, consequentially, diagnose infertility is not supported by the instant specification or the art of record. Nowhere in the instant disclosure can one find a credible assertion that infertility of any kind is associated with a reduction in the volume or mass of epididymis in humans. Therefore, one would not conclude that the quantitation of epididymis is useful in the diagnosis of infertility.

6) Claims 1 to 5, 17, 21 and 22 stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and practical asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7) Claims 1 to 3, 5 and 17 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention for those reasons of record in sections 5.1 and 5.2 of Paper Number 11.

7.1) Claims 1 to 3, 5 and 17 are vague and indefinite in reference to the term "derivative". Because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "derivative" of a protein having the amino acid sequence presented in SEQ ID NO:2 of the instant application an artisan can not determine if a compound which meets all of the other limitations of a claim, if any, would then be included or excluded from the claimed subject matter by the presence of this limitation.

7.2) Claims 2, 3 and 5 are vague and indefinite because they appear to be drawn to both a protein and a fragment, each of which appears to be an alternative embodiment of the other. Claim 1 is directed to a "protein", a "derivative" of a protein or a "fragment" of a protein. These appear to be three mutually exclusive embodiments of the claimed invention. Therefore, claims 2, 3 and 5 are confusing because they refer to the "protein of claim 1" as "said derivative or fragment".

8) Claims 1 to 5, 17, 21 and 22 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by the Osterhoff et al. publication (DNA and Cell Biol. 16(4):379-389, Apr. 1997) for those reasons of record in section 6 of Paper Number 11.

9) Applicant's arguments filed 23 December of 2002 have been fully considered but they are not persuasive for those reasons given above.

10) **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11) This application contains claims 6 to 16, 18 to 20 and 23 to 30 which are drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
PRIMARY EXAMINER
GROUP 1800